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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/810,490	MEHTALI ET AL.	
	Examiner	Art Unit	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/20/03*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-61* is/are pending in the application.

4a) Of the above claim(s) *60-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 March 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Election/Restriction

Initially, the examiner notes that the statement of pending claims in the restriction requirement was in error. The examiner indicated that claims 1-61 were pending when only claims 39-61 were pending at the time the restriction requirement was mailed.

Applicant's election with traverse of Group I, Claims 39-59 in the reply filed on 04/02/04 is acknowledged. The traversal is on the ground(s) that a search of the two groups would not be burdensome because claims 60 and 61 directly or indirectly depend from claim 39 of Group I and a search of one group would substantially, if not completely overlap, with a search of the other. This is not found persuasive because a search of Group II would not be co-extensive with a search of the subject matter of Group I. For example, a search of Group II would require a search of the gene therapy treatment arts whereas a search of Group I would not require a search of the gene therapy arts because no treatment methods are claimed in this Group. A search of each Group would require searching different classes and subclasses as well as different non-patent literature searches and searching both groups would be burdensome.

The requirement is still deemed proper and is therefore made FINAL.

Claims 60-61 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 04/02/04.

Priority

With regard to applicants' request that the amendment submitted on 3/19/01 with the transmittal letter be acknowledged, it is noted that said amendment has been entered. It is also noted that applicants only recited, in said amendment, a claim for benefit of the parent application 08/809,562, filed 3/31/97. If applicants seek to claim benefit for the PCT/FR96/01165 application (and hence provide continuity back to the French 95 08946 and 96 04413 applications), applicants must amend the first page of the specification (or supply a Application Data Sheet) to claim benefit for this PCT application.

It is noted that this application appears to claim subject matter disclosed in prior Application No. PCT/FR96/01165, filed 7/24/96. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. Also, the current status of all nonprovisional parent applications referenced should be included.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the

prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Abstract

The abstract of the disclosure is objected to because of the use of legal phraseology. The Abstract contains the legal phraseology "said vectors". Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 39-41, 49-59 are rejected under 35 U.S.C. 102(e) as being anticipated by Wilson et al. (US 5,856,152) or Wilson et al. (US 5,585,362).

Applicants claim a viral vector (and infectious viral particles comprising said vector) comprising an expression unit containing one or more viral genes, said

expression unit being functional in a complementation cell and nonfunctional in a host cell, and said vector comprising one or more heterologous regulator sequences (which can act at the level of transcription or translation) and an exogenous nucleotide sequence (which can be a sequence encoding a marker or CFTR, etc.). The expression unit comprises one or more regulatory sequences which activate the expression of said viral gene in the presence of an inducer. Applicants also claim a eukaryotic host cell comprising said infectious viral particle as well as a complementation cell (derived from 293 cells) which complements said viral vector function comprising a DNA coding for an inducer and which is capable of producing titers of greater than 5×10^8 pfu. Applicants also claim a method for preparing an infectious viral particle comprising introducing the aforementioned viral vector into a complementation cell and culturing the cells so as allow for production of the viral particles and harvesting the particles.

The examiner is interpreting the claims as follows: The "expression unit containing one of more viral genes" recited in the claims reads on a naturally occurring "expression unit" in a viral genome, i.e. a naturally occurring adenoviral E4 promoter and coding sequence in the context of an adenoviral vector genome. An "inducer" is defined by applicants (p. 10 of specification) as follows:

For the purposes of the present invention, the term "inducer" denotes a molecule which has the capacity of initiating or activating the expression of the viral genes placed under the control of a regulatory sequence, either directly by binding to said regulatory sequence, or indirectly via other cellular or viral factors. It can also prevent the action of a repressor. In contrast, a "repressor" has the capacity to inhibit or block the expression of the viral genes placed under the control of a regulatory sequence on which it acts, this taking place either directly or indirectly.

Given this definition of an inducer, adenoviral E1a would be an inducer of expression of other "expression units" in an adenoviral vector genome (i.e. E2 gene, E4 gene, etc.) since the adenoviral E1a gene product is a well known inducer of expression of adenoviral genes such as E2 , E4, etc.

Wilson et al. ('152 patent, see whole document, particularly Fig 1; column 3, lines 22-67; column 5, line 51 to column 9, line 36 and Example 4) and Wilson et al. ('362 patent, see whole document, particularly Fig. 3; column 3, line 21-column 4, line 53 and column 5, line 25-column 8, line 64) teach E1 region deleted adenoviral vectors (and adenoviral particles comprising said vectors) comprising expression units such as the adenoviral E4 gene promoter and coding regions wherein said expression units are functional in a complementation cell (i.e. 293 cells) which contains a DNA encoding and expressing the inducer (adenoviral E1a gene product) of expression of said adenoviral expression units and nonfunctional in a host cell (i.e. a non-293 cell) which does not express the E1a gene product. The adenoviral vectors (which can be produced at titers over 5×10^8 pfu) also comprise a heterologous gene which can be a marker or a sequence encoding CFTR, etc. under control of a heterologous promoter (i.e. CMV IE1 promoter). Wilson et al. also recite a complementation cell line (293 cells) which contains a DNA sequence encoding the E1a inducer, eucaryotic host cells infected with the adenoviral particles and a method for preparing an infectious adenoviral particle comprising introducing the adenoviral vector into a complementation cell, culturing the cell so as to produce the viral particle and harvesting the virus.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 39-59 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 and 31-42 of U.S. Patent No. 6,204,060 (hereafter the '060 patent). Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 39-59 are generic to all that is recited in claims 1-29 and 31-42 of the '060 patent. The claims of the '060 patent fall entirely within the scope of the instant claims. The instant claims recite generic viral vectors, viral particles, complementation cells comprising inducers, methods of making infectious viral particles, etc. wherein the claims of the '060 patent recite the species of adenoviral vectors, particles, complementation cell lines for generation of adenoviral vectors and particles, etc. The instant claims would be anticipated by the claims of the '060 patent.

35 USC 112, 1st Paragraph Rejections

Claims 39-59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim viral vectors comprising an expression unit containing one or more viral genes, said expression unit being functional in a complementation cell and nonfunctional in a host cell and comprising one or more heterologous regulator sequences as well as complementation cells which produce infectious viral particles at a titer of greater than 5×10^8 pfu, and methods of preparing an infectious viral particle. The claims read on a genus of viral vectors, particles and complementation cell lines as well as methods of making said viral particles. Applicants disclose adenoviral vectors, adenoviral particles and adenoviral vector complementation cells as well as methods of making infectious adenoviral particles with the recited characteristics.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention.

In the instant case, applicants provide no disclosure of any non-adenoviral vectors with the claimed characteristics, no disclosure of any non-adenoviral particles with the recited characteristics, no disclosure of any complementation cells for any non-adenoviral vectors and no disclosure of methods for generation of infectious non-adenoviral particles at the claimed titers. Applicants provide no correlation between the structure of the disclosed adenoviral vectors, particles and complementation cells and the structures of any other viral vectors, particles and complementation cells. Given the diversity of viruses involved (reading on viruses such as HCV, cosackieviruses, nodaviruses, polydnaviruses, etc.) most of which have not been previously recombinantly manipulated so as to express heterologous genes and for which no complementation cell lines exist, it must be concluded that the single example disclosed by applicants would not be considered by the skilled artisan to be a representative number of species sufficient to describe the claimed genus.

Claims 39-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for adenoviral vectors comprising an expression unit containing one or more viral genes wherein said expression unit is functional in a complementation cell and nonfunctional in a host cell and comprising one or more heterologous regulator sequences, adenoviral particles, complementation cells for said adenoviral vectors, and methods of preparing infectious adenoviral particles at the recited titers, does not reasonably provide enablement for any viral vectors, particles and complementation cells with the recited characteristics as well as making any

infectious viral particles at the recited titers. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants' invention is as described in the above 35 USC 112, 1st paragraph (enablement) rejection.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is required is not based upon a single factor, but rather is a conclusion reaches by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and include the following:
1) Unpredictability of the art. The art with regard to generating viral vectors comprising expression units containing one or more viral genes wherein said expression unit is functional in a complementation cell and nonfunctional in a host cell is unpredictable. The generation of complementation cells for viral vectors is unpredictable and often involves trial and error experimentation. For example, for many years the only complementation cell for generation of E1 deleted adenoviral vectors was the 293 cell line because, for unexplained reasons, only this cell could tolerate expression of the cytotoxic E1 gene products (E1a, E1b).
2) State of the art. The state of the art with regard to generation of viral vectors and complementation cell lines with the claimed characteristics was poorly developed.

3) Scope of the invention. The scope of the invention is broad, reading on any vectors and infectious particles derived from any virus and complementation cells for complementing replication of any virus vector.

4) Amount of guidance provided. Applicants provide no specific guidance on the generation of any non-adenoviral vector and complementing cell lines. Applicants provide no disclosure of starting materials, cell lines, culture conditions and methods for preparing viral vectors with the recited titers. The specification indicates that the skilled artisan, using prior art teachings, could reduce to practice the claimed invention with any virus system. However, the specification cannot merely rely on what was known in the art to provide an enabling disclosure of a claimed invention. As noted in *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001 (CAFC 1997):

> Rule that specification need not disclose what is well known in art means only that omission of minor details does not cause specification to fail to meet enablement requirement, and is not substitute for basic enabling disclosure; if there is no disclosure of any starting material or of any conditions under which claimed process can be carried out, undue experimentation is required, and there is failure to meet enablement requirement that cannot be rectified by asserting that all disclosure related to process is within skill of art.

5) Nature of the invention. The invention involves generation of recombinant expression systems from any virus and complementing cell lines for any viral vector.

6) Level of skill in the art. The level of skill in the art is high. However, given the broad scope of the claims, the lack of guidance provided by applicants and the unpredictability of the art, it must be considered that the skilled artisan would be reduced to conducting trial and error experimentation in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to have conducted undue and excessive experimentation in order to practice the claimed invention.

35 USC 112, 2nd Paragraph Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 39 (and dependent claims) are vague in that applicants recite a viral vector comprising an expression unit followed by the phrase "...and comprising one or more heterologous regulator sequences." It is unclear if this phrase relates to the vector or to the expression unit, i.e. whether the viral vector comprises one or more heterologous regulator sequences or whether the expression unit comprises one or more heterologous regulator sequences?

Claim 44 is vague in that applicants use abbreviations for different regulatory sequences without first spelling out the terms. Claim 44 is also vague in the recitation of the phrase "...bacterial **tryptophans lactose** (emphasis added) and tetracycline operons." It is assumed that applicants mean to recite "bacterial tryptophan, lactose and tetracycline operons"

Claims 45 and 46 are vague in that there is no antecedent basis for the term "said promoter" in the claim itself or the claim from which it depends.

Claim 50 is vague in that there is no antecedent basis for the term "the exogenous nucleotide sequence" in claim 39.

Claim 56 is vague in the recitation of the term "derived from" because it is unclear how close the cell "derived from" 293 cells is to the starting material (the original 293 cell). The metes and bounds of the subject matter are unclear.

Claim 59 is vague in that it is unclear if the composition recited is meant to comprise all of the first three elements together or each of them separately, i.e. are applicants reciting one composition comprising the viral vector, infectious viral particle and eucaryotic host cell together or separate compositions comprising the viral vector, a composition comprising the infectious viral particle and a composition comprising the eucaryotic cell.

It is noted that the Transmittal Papers filed 3/19/01 indicate that an Information Disclosure Statement (IDS) is enclosed. However, no IDS has been scanned into the file and no IDS is of record in the file.

The Drawings are objected to. Figures 1-11 are objected to because they do not contain numbers and reference characters at least 1/8 inch in height (37 CFR 1.84(p)(3)). Figures 1-11 have numbers and reference characters which are not plain and legible (37 CFR 1.84(p)). Figure 12 is very dark and unintelligible. Corrected

drawings must be submitted in applicants' response to this Office Action. Any response which does not include acceptable substitute drawings will be considered non-responsive.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, PhD., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DAVID GUZO
PRIMARY EXAMINER

David Guzo
June 7, 2004

JASEMINE C. CHAMBERS
DIRECTOR
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